

What is claimed is:

1. A device for detecting the presence of an analyte in a fluid sample, the device comprising a solid substrate microfabricated to define:
  - a sample inlet port; and
  - a mesoscale flow system comprising:
    - a sample flow channel extending from said inlet port; and
    - an analyte detection region in fluid communication with said flow channel comprising a binding moiety for specifically binding said analyte, said detection region having a mesoscale dimension.
2. The device of claim 1 wherein said binding moiety is immobilized in said detection region.
3. The device of claim 1, wherein the device further includes a window for optically probing said detection region disposed over said region on said substrate.
4. The device of claim 1 wherein said substrate further defines means for delivering to said detection region a labeled substance which binds to said analyte to produce a detectable signal indicative of the presence of said analyte.
5. The device of claim 4 further comprising:
  - a window for optically probing said detection region disposed over said region on said substrate; and
  - optical means for detecting the presence of said detectable signal through said window.

6. The device of claim 1 wherein said analyte is an antigen and said binding moiety is an antigen binding protein.

7. The device of claim 1 wherein said analyte is a polynucleotide and said binding moiety is a complementary polynucleotide which hybridizes with said polynucleotide.

8. The device of claim 1 wherein said analyte and said immobilized binding moiety comprise a ligand/receptor pair.

9. The device of claim 4 wherein said optically detectable signal is a luminescent signal.

10. The device of claim 9 wherein said optically detectable signal is a fluorescent signal.

11. The device of claim 3 wherein said analyte detection region comprises particles having analyte binding sites on the surface thereof which, in the presence of an analyte induce particle agglomeration optically detectable through said window.

12. The device of claim 3 wherein said substrate further defines a control region in fluid communication with said sample inlet port and a control region window, disposed over said control region on said substrate, for optically probing said control region whereby data determined optically in said control and detection regions may be compared.

13. The device of claim 3 wherein said analyte is a cell population in said sample, and wherein said binding moiety binds to a surface protein on members of said cell population to induce agglutination of said cell population; and said agglutination is optically detectable through said window.

14. The device of claim 1 wherein said substrate defines at least a second mesoscale flow system.

15. The device of claim 14 wherein the analyte detection regions of said flow systems comprise different immobilized binding moieties.

16. The device of claim 1, wherein the analyte is an intracellular molecular component in a cell-containing liquid biological sample, the device further comprising:

cell lysing means in said mesoscale flow system in fluid communication with said flow channel; and

means for forcing cells in said cell-containing microsample within said substrate into said cell lysing means thereby to release said intracellular molecular component.

17. The device of claim 16 wherein said cell lysing means comprises a portion of said flow channel having cell-membrane piercing protrusions extending from a wall thereof.

18. The device of claim 16 wherein said cell lysing means comprises a region of restricted cross-sectional dimension sufficient to permit passage of intracellular molecules while prohibiting passage of cells.

19. The device of claim 1, wherein said analyte is a cell population in said sample, said device further comprising:

- a cell separation region comprising sites for binding cell surface protein immobilized on a wall of said separation region; and

- means for inducing flow of said microsample to said separation region:

- at a first flow rate sufficiently slow to permit capture of said cell population in the sample by said binding sites to separate said cell population from said microsample; and

- at a second, higher, flow rate sufficient to release said separated cell fraction from said region.

20. The device of claim 3 wherein said flow system further comprises:

- a fractal region in fluid communication with said flow channel comprising bifurcations leading to plural secondary flow channels; and

- means for inducing flow of a biological sample through said flow channel and said fractal region.

21. The device of claim 1 wherein said solid substrate comprises microfabricated silicon.

22. The device of claim 1 wherein said sample flow channel and said detection region are microfabricated in a surface of a solid substrate and enclosed by a cover adhered to said surface.

23. The device of claim 1 further comprising an appliance for use in combination with said substrate, said appliance comprising:

means for holding said substrate,  
fluid input means interfitted with an inlet port on said substrate, and  
pump means for passing fluid through the flow system of said substrate when it is held in said holding means.

24. The device of claim 23 wherein said appliance further comprises a reagent reservoir and means for delivering a reagent to said flow system.

25. The device of claim 1, further comprising an appliance for use in combination with said substrate, said appliance comprising:

means for holding said substrate; and  
optical means for viewing the contents of said mesoscale flow system in said substrate.

26. The device of claim 25, wherein said optical means comprises magnifying optics and a video camera, and wherein said appliance further comprises:

a tilt mechanism for manually adjusting the angle and location of the device; and  
a video screen for viewing the contents of said flow system.

27. A method for detecting the presence of an analyte in a fluid sample, the method comprising the steps of:

- (i) providing a device comprising a solid substrate microfabricated to define:
  - a sample inlet port; and
  - a mesoscale flow system comprising:
    - a sample flow channel extending from said inlet port; and
    - an analyte detection region in fluid communication with said flow channel comprising a binding moiety for specifically binding said analyte, said detection region having a mesoscale dimension;
- (ii) delivering said sample to said inlet port and through said flow system to said detection region; and
- (iii) detecting the binding of said analyte to said binding moiety in said detection region.

28. The method of claim 27 wherein said binding moiety in the device provided in step (i) is immobilized in said detection region; and

wherein step (iii) includes the step of detecting the binding of said analyte and said immobilized binding moiety.

29. The method of claim 27, wherein the device provided in step (i) further includes a window disposed over said detection region on said substrate; and

wherein step (iii) includes the step of optically probing said detection region through said window.

30. The method of claim 27 wherein the device provided in step (i) further includes means for delivering to said detection region a labeled substance which binds to said analyte to produce a detectable signal indicative of the presence of said analyte, the method further comprising:

- (iv) delivering a labeled substance to said detection region; and
- (v) optically probing for said detectable signal in said detection region.

31. The method of claim 30 wherein said optical probing step includes the step of detecting a luminescent signal.

32. The method of claim 27 wherein said analyte detection region, in the device provided in step (i), comprises particles having analyte binding sites on the surface thereof which, in the presence of an analyte, induce particle agglomeration;

wherein, in step (ii), said analyte binds to said particles to induce agglomeration; and

wherein, in step (iii), agglomeration is detected.

33. The method of claim 29 wherein said substrate provided in step (i) further defines a control region in fluid communication with said sample inlet port and a control region window, disposed over said control region on said substrate, for optically probing said control region whereby data determined optically in said control and detection regions may be compared; and

wherein step (iii) includes the step of optically probing and comparing said control region and said detection region.

34. The method of claim 29 wherein said analyte is a cell population in said sample, and wherein,

in step (ii), said binding moiety binds to a surface protein on members of said cell population to induce agglutination of said cell population; and

in step (iii), said agglutination is optically detected through said window.

35. The method of claim 27 wherein said substrate, provided in step (i), defines at least a second said mesoscale flow system; and

wherein, in step (iii), binding in the detection regions in said first and at least second system is detected.

36. The method of claim 27, wherein the analyte is an intracellular molecular component in a cell-containing liquid biological sample, said method comprising the additional step of lysing said cells within said substrate to release said intracellular analyte prior to step (iii).

37. The method of claim 27, wherein said analyte is a cell population in said sample, said method comprising the additional step of separating said cell population from other cells within said substrate prior to step (iii).



38. An appliance for use with an analytical device including a solid substrate microfabricated to define at least one inlet port and a mesoscale flow system, extending from an inlet port on said substrate, the appliance comprising:

means for holding said substrate;

fluid input means interfitted with an inlet port on said substrate; and

pump means for passing fluid through the flow system of said substrate when is held in said holding means.

39. The appliance of claim 38, further comprising a reagent reservoir and means for delivering a reagent to said flow system.

40. The appliance of claim 39, further comprising detection means for detecting a parameter of a fluid sample in said flow system.

41. The device of claim 1, wherein said analyte detection region comprises a tortuous mesoscale flow channel; and

wherein said tortuous channel is microfabricated with a length allowing the timed mixing and reaction of fluid flowing through said tortuous channel.

42. The method of claim 27, wherein said analyte detection region further comprises a tortuous mesoscale flow channel, upstream from said detection reaction;

wherein said tortuous channel is microfabricated with a length allowing the timed mixing and reaction of fluid flowing through said tortuous channel prior to delivery to said detection region; and

wherein step (ii) includes the step of delivering said sample to said tortuous channel then to said detection region.